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L78 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:465749** HCAPLUS
DN **137:46052**
TI Immunogenic **cancer** peptides: diagnosis and therapy
IN **Calenoff, Emanuel; Ditlow, Charles C.**
PA Northwestern University, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 8, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047613	A2	20020620	WO 2001-US47734	20011113
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002043314	A5	20020624	AU 2002-43314	20011113
PRAI	US 2000-723307	A	20001127		
	WO 2001-US47734	W	20011113		

AB The author discloses general methods and compns. that provide **cancer-specific** or highly **cancer-assocd. antigens** useful for diagnosis and treatment of **cancer.** The **antigens** are identified by their loss of

glycosylation on **tumors** vs. normal tissue with or without further modification (phosphorylation).

ST **cancer antigen** peptide diagnosis therapy

IT CD **antigens**
RL: PRP (Properties)
(CD66; identification of **extracellular domain**-derived **cancer-assocd.** and **cancer-specific** peptides)

IT Cadherins
RL: PRP (Properties)
(E-; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT Immunoglobulins
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(G; to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens**)

IT Cadherins
RL: PRP (Properties)
(N-; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT Imaging
(NMR; with proteins binding to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens** for)

IT **Peptides**, biological studies
RL: ANT (Analyte); ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(asparagine-contg.; of **extracellular domain** of **cancer-specific** and **cancer-assocd. antigens** in relation to diagnosis and therapy)

IT Cell adhesion molecules
Proteins
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(binding to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens** by)

IT Diagnosis
(**cancer**; **extracellular domain**-derived peptides of **cancer antigens**)

IT **Peptides**, biological studies
RL: ANT (Analyte); ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**deglycosylated**; of **extracellular domain** of **cancer-specific** and **cancer-assocd. antigens** in relation to diagnosis and therapy)

IT **Neoplasm**
(diagnosis; **extracellular domain**-derived peptides of **cancer antigens**)

IT **Tumor** markers
(**extracellular domain**-derived peptides of **cancer antigens**)

IT **Algorithm**
(for identification of **extracellular domain**-derived peptides of **cancer antigens**)

IT Immunoglobulins

RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fragments; to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens**)

IT **Protein motifs**
(**glycosylation** site; is absent for **extracellular domain**-derived **peptides** of **cancer-specific** and **cancer-assocd. antigens**)

IT CD40 (**antigen**)
CD44 (**antigen**)
Epidermal growth factor receptors
neu (receptor)
RL: PRP (Properties)
(identification of **extracellular domain**-derived **cancer-assocd.** and **cancer-specific** peptides)

IT Antibodies
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens**)

IT Prostate gland
(**neoplasm**; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT Immunoassay
(of antibodies to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens**)

IT Phosphopeptides
RL: ANT (Analyte); ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(of **extracellular domain** of **cancer-specific** and **cancer-assocd. antigens** in relation to diagnosis and therapy)

IT Phosphorylation, biological
(protein; of **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens**)

IT **Antitumor** agents
(proteins binding to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens**)

IT **Carcinoma**
(squamous cell; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT Antibodies
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd**. **antigens**)

IT **Antigens**
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(**tumor-assocd.**; identification and application of **extracellular domain**-derived peptides of)

IT **Antigens**

RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(**tumor-specific antigens**; identification and application of **extracellular domain**-derived peptides of)

IT Vaccines
(**tumor**; **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens**)

IT Imaging
(**tumor**; proteins binding to **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd. antigens** for)

IT **Antitumor** agents
(vaccines; **extracellular domain**-derived peptides of **cancer-specific** and **cancer-assocd**. **antigens**)

IT Integrins
RL: PRP (Properties)
(.alpha.v; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT Integrins
RL: PRP (Properties)
(.alpha.3; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT Transforming growth factor receptors
RL: PRP (Properties)
(.beta.-transforming growth factor type II; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT Integrins
RL: PRP (Properties)
(.beta.1; identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT 437614-84-1 437614-85-2 437614-86-3 437614-87-4 437614-88-5
437614-89-6 437614-90-9 437614-91-0 437614-92-1 437614-93-2
437614-94-3 437614-95-4 437614-96-5 437614-97-6 437614-98-7
437614-99-8 437615-00-4 437615-01-5
RL: PRP (Properties)
(identification of **extracellular domain**-derived **cancer**-assocd. and **cancer**-specific peptides)

IT 437975-00-3
RL: PRP (Properties)
(unclaimed sequence; immunogenic **cancer** peptides, diagnosis and therapy)

L78 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:185159** HCAPLUS
DN **136:244041**
TI A method for identifying peptide sequences having a specific functionality
IN Schneider, Gisbert; Eichler-Mertens, Mathias; Wrede, Paul
PA Callistogen A.-G., Germany
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-00
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 34
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2002020564 A2 20020314 WO 2001-EP10195 20010905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2001093794 A5 20020322 AU 2001-93794 20010905
PRAI US 2000-655056 A 20000905
WO 2001-EP10195 W 20010905

AB The present invention relates to a method for creating a sequence-function relationship, a method for identifying or generating peptide sequences having a specific functionality, using the created sequence-function relationship and a method for generating a focussed synthetic peptide library. The PepHarvester algorithm was applied to the HSP70 binding peptide LHIYTT. By using a diversity index of 0.1, 40 variants were created.

ST peptide sequence specific function relationship; PepHarvester algorithm HSP70 binding peptide variant creation

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA, class I; method for identifying peptide sequences having a specific functionality)

IT Heat-shock **proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HSP 70, peptides binding to; method for identifying peptide sequences having a specific functionality)

IT p53 (**protein**)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(HSP70-binding peptides of; method for identifying peptide sequences having a specific functionality)

IT **Proteins**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(MART-1, MHC class I-binding tumor-specific peptide of, as seed peptide; method for identifying peptide sequences having a specific functionality)

IT Histocompatibility **antigens**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), class I, **tumor-specific** peptide of MART-1 binding to; method for identifying peptide sequences having a specific functionality)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), peptides binding to; method for identifying peptide sequences having a specific functionality)

IT Neoplasm
(MHC class I-binding tumor-specific peptides creation; method for identifying peptide sequences having a specific functionality)

IT **Algorithm**
(PepHarvester; method for identifying peptide sequences having a specific functionality)

IT Angiotensin receptor antagonists
(angiotensin II; method for identifying peptide sequences having a specific functionality)

IT Vasopressin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists or agonists; method for identifying peptide sequences

having a specific functionality)
IT **Protein motifs**
(cleavage sites; method for identifying peptide sequences having a specific functionality)
IT T cell (lymphocyte)
(cytotoxic, peptide epitope sequences induction in human of; method for identifying peptide sequences having a specific functionality)
IT Bioassay
(identified peptide sequences testing in; method for identifying peptide sequences having a specific functionality)
IT Biological transport
Dopamine agonists
Dopamine antagonists
Drug design
Epitopes
Human
Hydrophilicity
Hydrophobicity
Peptide library
Physical properties
Polarity
Protein sequences
Refractive index
Statistical analysis
Structure-activity relationship
Surface area
Vaccines
Volume
(method for identifying peptide sequences having a specific functionality)
IT Endothelin receptors
Hormone receptors
Neuropeptides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for identifying peptide sequences having a specific functionality)
IT **Peptides**, biological studies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for identifying peptide sequences having a specific functionality)
IT **Amino acids**, properties
RL: PRP (Properties)
(method for identifying peptide sequences having a specific functionality)
IT Evolution
(mol.; method for identifying peptide sequences having a specific functionality)
IT **Simulation and Modeling, biological**
Simulation and Modeling, physicochemical
(neural network; method for identifying peptide sequences having a specific functionality)
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide inhibitors of assembly of; method for identifying peptide sequences having a specific functionality)
IT Stability
(peptide; method for identifying peptide sequences having a specific functionality)
IT G **protein**-coupled receptors
Heat-shock **proteins**
Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptides binding to; method for identifying peptide sequences having a specific functionality)

IT Human immunodeficiency virus
(receptors, peptides binding to; method for identifying peptide sequences having a specific functionality)

IT **Molecular structure-property relationship**
(stability, peptide; method for identifying peptide sequences having a specific functionality)

IT Immunization
(vaccination; method for identifying peptide sequences having a specific functionality)

IT 403666-90-0 403666-91-1 403666-92-2 403666-93-3 403666-94-4
403666-95-5 403666-96-6 403666-97-7 403666-98-8 403666-99-9
403667-00-5 403667-01-6 403667-02-7 403667-03-8 403667-04-9
403667-05-0 403667-06-1 403667-07-2 403667-08-3 403667-09-4
403667-10-7 403667-11-8 403667-12-9 403667-13-0 403667-14-1
403667-15-2 403667-16-3 403667-17-4 403667-18-5 403667-19-6
403667-20-9 403667-21-0 403667-22-1 403667-23-2 403667-24-3
403667-25-4 403667-26-5 403667-27-6 403667-28-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence, PepHarvester algorithm-generated HSP70-binding peptide; method for identifying peptide sequences having a specific functionality)

IT 403666-69-3 403666-70-6 403666-71-7 403666-72-8 403666-73-9
403666-74-0 403666-75-1 403666-76-2 403666-77-3 403666-78-4
403666-79-5 403666-80-8 403666-81-9 403666-82-0 403666-83-1
403666-84-2 403666-85-3 403666-86-4 403666-87-5 403666-88-6
RL: PRP (Properties)
(amino acid sequence, PepHarvester algorithm-generated MHC class I-binding tumor-specific peptide; method for identifying peptide sequences having a specific functionality)

IT 403666-89-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence, as HSP70-binding seed peptide; method for identifying peptide sequences having a specific functionality)

IT 156251-11-5
RL: PRP (Properties)
(amino acid sequence, as MHC class I-binding tumor-specific seed peptide; method for identifying peptide sequences having a specific functionality)

IT 156250-93-0 156251-12-6 156251-13-7 403667-29-8 403667-30-1
403667-31-2 403667-32-3 403667-33-4
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence, as calcd. HLA-0201 epitope of MART-1 protein; method for identifying peptide sequences having a specific functionality)

IT 220087-98-9 403667-34-5 403667-35-6 403667-36-7 403667-37-8
403667-38-9 403667-39-0 403667-40-3 403667-41-4 403667-42-5
403667-43-6 403667-44-7 403667-45-8 403667-46-9 403667-47-0
403667-48-1 403667-49-2 403667-50-5 403667-51-6 403667-52-7
403667-53-8 403667-54-9 403667-55-0 403667-56-1 403667-57-2
403667-58-3 403667-59-4 403667-60-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence, as calcd. HSP70-binding peptide in protein p53; method for identifying peptide sequences having a specific functionality)

IT 9015-82-1, ACE
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors, peptides binding to; method for identifying peptide sequences having a specific functionality)

IT 37259-58-8, Serine protease 37353-41-6, Cysteine protease 78169-47-8, Aspartylprotease 81669-70-7, Metalloprotease 158736-49-3, .beta.-Secretase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; method for identifying peptide sequences having a specific functionality)

IT 9001-92-7, Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prediction of cleavage sites for; method for identifying peptide sequences having a specific functionality)

IT 267000-55-5 404012-83-5 404012-84-6 404012-85-7
RL: PRP (Properties)
(unclaimed sequence; method for identifying peptide sequences having a specific functionality)

L78 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:52467 HCAPLUS
DN 136:245335
TI Dysadherin, a cancer-associated cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis
AU Ino, Yoshinori; Gotoh, Masahiro; Sakamoto, Michiie; Tsukagoshi, Kiyomi; Hirohashi, Setsuo
CS Pathology Division, National Cancer Center Research Institute, Tokyo, 104-0045, Japan
SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(1), 365-370
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 6, 13
AB The authors report the cloning and characterization of a **cancer-assocd.** cell membrane glycoprotein recognized by mAb NCC-3G10. The antibody showed strong reactivity to a wide variety of cancer cells, but only to a limited no. of normal cells including lymphocytes, endothelial cells, and basal cells of stratified squamous epithelium. The cDNA for the **antigen** encodes 178 aa, which includes a putative signal sequence, a potential O-**glycosylated extracellular domain**, a single transmembrane domain, and a short cytoplasmic tail. Transfection of the cDNA into PLC/PRF/5 liver cancer cells resulted in reduced cell-cell adhesiveness, based on both morphol. and results of Ca2+-dependent cell aggregation assay. In transfected cells, E-cadherin was markedly decreased at the **protein** level in inverse proportion to the expression level of the **antigen** recognized by NCC-3G10, but not at the mRNA level. Aggregation of the **antigen** by NCC-3G10-coated beads triggered accumulation of actin, suggesting some interplay between this **antigen** and E-cadherin through actin. When metastatic ability was examd. in severe combined immunodeficient mice by injecting PLC/PRF/5 cells into the spleen, the transfectants formed a markedly higher no. of metastatic nodules in comparison with controls. The authors have named this cell membrane glycoprotein, which down-regulates E-cadherin and promotes metastasis, dysadherin.
ST dysadherin cancer assocd plasma membrane E cadherin downregulation metastasis; sequence dysadherin cDNA human
IT Cadherins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(E-; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)

IT Skin
(basal cell; dysadherin, cancer-assocd. cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis in relation to expression in limited no. of normal cells)

IT Cell membrane
Human
Liver, neoplasm
Lung, neoplasm
Neoplasm
Protein sequences
Stomach, neoplasm
cDNA sequences
(cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)

IT Cell adhesion
Protein motifs
Self-association
(cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis in relation to)

IT Actins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis in relation to)

IT Cell aggregation
(calcium-dependent; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis in relation to)

IT Uterus, neoplasm
(cervix; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)

IT Intestine, neoplasm
(colon; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(dysad; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)

IT New natural products
(dysadherin (protein))

IT T cell (lymphocyte)
(dysadherin, cancer-assocd. cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis in relation to expression in limited no. of normal cells)

IT **Proteins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); NPO (Natural product occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(dysadherin; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)

IT Blood vessel
(endothelium; dysadherin, cancer-assocd. cell membrane glycoprotein, down-regulates E-cadherin and promotes metastasis in relation to expression in limited no. of normal cells)

IT Neoplasm
(metastasis; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)

IT Bladder
Esophagus
Mammary gland
(neoplasm; cDNA sequence of dysadherin, cancer-assocd. cell membrane

glycoprotein, that down-regulates E-cadherin and promotes metastasis)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-dependent cell aggregation; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis in relation to)
IT 403976-61-4
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); NPO (Natural product occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
IT 386529-39-1, GenBank AB072911
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; cDNA sequence of dysadherin, cancer-assocd. cell membrane glycoprotein, that down-regulates E-cadherin and promotes metastasis)
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L78 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:756972** HCAPLUS
DN **133:320994**
TI Improved method of identifying and locating immunobiologically-active linear peptides
IN Kokolus, William J.
PA USA
SO PCT Int. Appl., 39 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-53
ICS C12P021-00; C07K001-00; A61K039-00
CC 15-2 (Immunochemistry)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000063693	A1	20001026	WO 2000-US10585	20000419
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1179178	A1	20020213	EP 2000-928224	20000419
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-130230P	P	19990420		
	US 2000-552461	A	20000418		
	WO 2000-US10585	W	20000419		

AB The present invention relates to identifying protein epitopes and more particularly to a novel method for identifying, detg. the location, optimal length of amino acid residues and immunobiol. potency of protein epitopes by fitting a hydrophilicity and/or hydrophobicity plot generated for the amino acid linear sequence of a polypeptide to a math. generated continuous curve thereby generating at least one set of potential epitopes which include ranked potential epitopes having a specific no. of amino acid residues. The immunobiol.-active linear peptides are deemed the potential epitopes that exhibit the most alternating positioning about an equil. position when juxtaposed on the hydrophilicity and/or hydrophobicity plot and their optimal length corresponds to the specific no. of amino acid residues in the set of ranked potential epitopes. The amino acid sequence of the protein epitopes of the present invention exhibit a hydrophobic-hydrophilic-hydrophobic motif. The method may be used to select hydrophobic-hydrophilic-hydrophobic epitopes from cancer cells, viral, microbial and other mols. of basic and clin. research interest in lymphokines and interferons, cluster differentiation antigen and MHC antigens, hormones and growth factors, tumor markers and tumor suppressors, oncogenes, viral antigens, and nuclear matrix proteins.

ST antigen epitope identification; hydrphobicity hydrophilicity curve antigen protein motif

IT Hydrophilicity
(Kyte-Doolittle hydropathy value; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Histocompatibility antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex); improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Animal virus
Microorganism
(antigen; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Mathematical methods**
(**curve**; improved method comprising math. generated

curve for identifying and locating immunobiol.-active linear peptides)

IT Antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(differentiation, cluster; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Reaction
(equation; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Protein motifs**
(hydrophobic-hydrophilic-hydrophobic; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Prostate-specific antigen
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(immunogenic epitope; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Antiserums
Epitopes
Hydrophobicity
Tumor markers
(improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Antigens
Growth factors, animal
Hormones, animal, biological studies
Interferons
Lymphokines
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Proteins**, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nuclear matrix-assocd.; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Gene
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(oncogene; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT Diagnosis
(testing; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Proteins**, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(tumor suppressor; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

IT **Antigens**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**tumor-assocd.**; improved method comprising math.
generated curve for identifying and locating immunobiol.-active linear peptides)

IT 75037-46-6, Gelonin
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(immunogenic epitope; improved method comprising math. generated curve for identifying and locating immunobiol.-active linear peptides)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(3) Kyte; J Mol Biol 1982, V157, P105 HCAPLUS

L78 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:764292** HCAPLUS
DN **132:22170**
TI Identification of peptides with degenerate HLA-DR binding specificity
IN Sette, Alessandro; Southwood, Scott; Sidney, John
PA Epimmune, Inc., USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-574
ICS G01N033-53; C12N007-00; A61K039-42; A61K039-395; A61K039-21; A61K039-29; C07K016-00
CC 15-2 (Immunochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961916	A1	19991202	WO 1999-US12066	19990528
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2332786	AA	19991202	CA 1999-2332786	19990528
	AU 9942244	A1	19991213	AU 1999-42244	19990528
	EP 1080370	A1	20010307	EP 1999-926084	19990528
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002516824	T2	20020611	JP 2000-551261	19990528
PRAI	US 1998-87192P	P	19980529		
	WO 1999-US12066	W	19990528		

AB The authors analyzed the peptide binding specificity of a set of 13 different DR mols., representative of DR types common among the worldwide population. Detailed maps of secondary anchors and secondary interactions were derived for three of them (DR4w4, DR1 and DR7). Furthermore, the authors demonstrated that a set of at least seven different DR types share overlapping peptide binding repertoires; and consequently that broadly degenerate HLA DR binding peptides are a relatively common occurrence. This study also describes computerized procedures which should greatly assist in the task of identification of such degenerate peptides.
ST peptide epitope degeneracy HLA DR
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR, HLA-DR12; identification of peptides with degenerate HLA-DR binding specificity)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR, HLA-DR13; identification of peptides with degenerate HLA-DR binding specificity)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(HLA-DR, HLA-DR51; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR, HLA-DR53; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR1; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR2; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR3; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR4; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR6; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR7; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR8; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DR9; identification of peptides with degenerate HLA-DR binding specificity)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-DRw11; identification of peptides with degenerate HLA-DR binding specificity)

IT **Peptides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analogs; with degenerate HLA-DR binding specificity)

IT T cell (lymphocyte)
(cytotoxic; peptides with degenerate HLA-DR binding specificity for stimulation of)

IT Carcinoembryonic antigen
neu (receptor)

p53 (**protein**)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(degenerate HLA-DR binding specificity for peptides of)

IT Hepatitis B virus
Hepatitis C virus
Human immunodeficiency virus
Plasmodium falciparum
(degenerate HLA-DR binding specificity for peptides of antigens of)

IT Synthetic gene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for HLA-DR-restricted peptides)

IT **Algorithm**
(for identification of peptides with degenerate binding specificity for HLA-DR)

IT **Protein motifs**
(for peptides binding HLA-DR mols.)

IT T cell (lymphocyte)
(helper cell; peptides with degenerate HLA-DR binding specificity for stimulation of)

IT Epitopes
(identification of peptides with degenerate HLA-DR binding specificity)

IT Vaccines
(synthetic; peptides with degenerate HLA-DR binding specificity in relation to)

IT **Antigens**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tumor-assocd.**, MAGE-2; degenerate HLA-DR binding specificity for peptides of)

IT **Antigens**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tumor-assocd.**, MAGE-3; degenerate HLA-DR binding specificity for peptides of)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(viral; degenerate HLA-DR binding specificity for peptides of)

IT **Peptides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(with degenerate HLA-DR binding specificity)

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207344-59-0 207344-63-6 207344-64-7 211050-94-1 211051-04-6
211051-15-9 211051-25-1 211051-55-7 251545-14-9 251545-16-1
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RL: PRP (Properties)
(Unclaimed; identification of peptides with degenerate HLA-DR binding specificity)

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RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(identification of peptides with degenerate HLA-DR binding specificity)

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RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(identification of peptides with degenerate HLA-DR binding specificity)

IT 251544-91-9 251544-92-0 251544-93-1 251544-94-2 251544-95-3
251544-96-4 251544-97-5 251544-98-6 251545-00-3 251545-01-4
251545-02-5 251545-03-6 251545-04-7 251545-05-8 251545-06-9
251545-07-0 251545-08-1 251545-09-2 251545-11-6 251545-12-7
251545-13-8 251661-56-0 251661-57-1 251661-58-2 251661-59-3
251661-60-6 251661-64-0 251973-65-6
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(identification of peptides with degenerate HLA-DR binding specificity)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bremers; J Immunotherapy 1995, V18(2), P77 HCAPLUS
(2) Fraziano; Clinical Immunology and Immunopathology 1997, V84(2), P202 MEDLINE
(3) Harrison; J Exp Med 1997, V185(6), P1013 HCAPLUS
(4) Ras; Human Immunology 1997, V53, P81 HCAPLUS
(5) Valmori; Cancer Research 1997, V57(4), P735 HCAPLUS
(6) Zaremba; Cancer Research 1997, V57, P4570 HCAPLUS

L78 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:639411 HCAPLUS
DN 127:306411
TI Molecular cloning of a monoclonal anti-tumor antibody specific for the Tn antigen and expression of an active single-chain Fv fragment
AU Babino, Alvaro; Pritsch, Otto; Oppezzo, Pablo; Du Pasquier, Renaud; Roseto, Alberto; Osinaga, Eduardo; Alzari, Pedro M.
CS Departamento de Bioquimica, Facultad de Medicina, Montevideo, Urug.
SO Hybridoma (1997), 16(4), 317-324
CODEN: HYBRDY; ISSN: 0272-457X
PB Liebert
DT Journal
LA English
CC 15-3 (Immunochemistry)
Section cross-reference(s): 14
AB The authors report here the first **amino acid** sequence of an anti-Tn monoclonal antibody raised against human breast cancer cells

and show that a single chain Fv fragment of this IgM retains the Tn-binding specificity as defined by functional assays with asialo-OSM and membrane exts. from MCF-7 cells. Sequence comparisons and mol. modeling of 83D4 indicate that the antibody combining site displays a cavity-like feature primarily defined by the CDR H1 and H2 loops. This pocket could accommodate a single Tn mol., thus, suggesting a structural explanation for the predominant expression of a particular VH gene segment in a group of antibodies that recognize **tumor-assocd. antigens** arising from an aberrant O-**glycosylation**.

ST monoclonal antibody Tn tumor antigen; scFv antibody Tn breast tumor

IT Gene, animal
RL: PRP (Properties)
(Igh; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT Gene, animal
RL: PRP (Properties)
(Ig.kappa.; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(M, monoclonal; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT Blood-group substances
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Tn; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT **DNA sequences**
Protein sequences
(cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT Immunoglobulins
RL: PRP (Properties)
(heavy chains, .mu.; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT Immunoglobulins
RL: PRP (Properties)
(light chains, .kappa.; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT Mammary gland
(neoplasm; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT **Molecular modeling**
(of monoclonal anti-Tn antibody)

IT Antibodies
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(single chain, scFv; cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

IT 14215-68-0D, .alpha.-N-Acetylgalactosamine, glycoproteins expressing
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cloning of monoclonal anti-Tn antibody and expression of scFv fragment)

L78 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1986:219959 HCAPLUS
DN 104:219959
TI Primary structure of the human melanoma-associated antigen p97 (melanotransferrin) deduced from the mRNA sequence
AU Rose, Timothy M.; Plowman, Gregory D.; Teplow, David B.; Dreyer, William

J.; Hellstroem, Karl Erik; Brown, Joseph P.
CS ONCOGEN, Seattle, WA, 98121, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1986), 83(5), 1261-5
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 13, 14, 15
AB Cell-surface glycoprotein p97 is present in most human melanomas but only in trace amts. in normal adult tissues. To det. the structure of this **tumor-assocd. antigen** and to identify its functional domains, p97 mRNA was purified, cloned, and its nucleotide sequence detd. The mRNA encodes a 738-residue precursor, which contains the previously detd. N-terminal **amino acid** sequence of p97. After removal of a 19-residue signal **peptide**, the mature p97 mol. comprises **extracellular domains** of 342 and 352 residues and a C-terminal 25-residue stretch of predominantly uncharged and hydrophobic **amino acids** which acts as a membrane anchor. Each **extracellular domain** contains 14 cysteine residues, which form 7 intradomain disulfide bridges, and 1-2 potential **N-glycosylation** sites. Protease digestion studies show that the 3 major **antigenic** determinants of p97 are present on the N-terminal domain. The domains are strikingly homologous to each other (46% **amino acid** sequence homol.) and to the corresponding domains of human serum transferrin (39% homol.). Conservation of disulfide bridges and of **amino acids** thought to compose the iron-binding pockets suggests that p97 is also related to transferrin in tertiary structure and function. Glycoprotein p97 should be renamed melanotransferrin to denote its original identification in melanoma cells and its evolutionary relationship to serotransferrin and lactotransferrin, the other members of the transferrin superfamily.
ST human melanoma glycoprotein p97 cDNA sequence; melanotransferrin gene sequence human melanoma; cloning sequence glycoprotein p97 mRNA human
IT Melanoma
(antigen p97 of, of human, structure of)
IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(for antigen p97, of human melanoma cell, nucleotide and encoded peptide sequences of)
IT Transferrins
RL: BIOL (Biological study)
(glycoprotein antigen p97 of human melanoma structural homol. with)
IT **Protein** sequences
(of glycoprotein antigen p97 and precursor, of human melanoma, complete)
IT Molecular cloning
(of glycoprotein antigen p97 cDNA, of human melanoma cells)
IT Ribonucleic acids, messenger
RL: PROC (Process)
(antigen p97-specifying, of human melanoma cells, purifn. of)
IT **Deoxyribonucleic acid sequences**
(antigen p97-specifying, of human, complete)
IT Transferrins
RL: BIOL (Biological study)
(melano-, glycoprotein antigen p97 of human melanoma as)
IT Antigens
RL: BIOL (Biological study)
(p97, of human melanoma cells, structure of)
IT 102347-16-0 102347-17-1
RL: PRP (Properties)
(amino acid sequence of)

IT 102347-28-4
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence of)

=> fil medline
FILE 'MEDLINE' ENTERED AT 15:13:54 ON 19 NOV 2002

FILE LAST UPDATED: 16 NOV 2002 (20021116/UP). FILE COVERS 1958 TO DATE.

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MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

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=> d all tot

L121 ANSWER 1 OF 4 MEDLINE
AN **2002325926** MEDLINE
DN **22045525** PubMed ID: **12050499**
TI Evaluation of a new serum testing method for detection of prostate cancer.
AU Seabury Charles A; **Calenoff Emanuel; Ditlow Charles;**
Bux Sajit; Clarke Harry; Issa Muta; Marshall Fray; Petros John
CS Emory University, Atlanta, Georgia, USA.
SO JOURNAL OF UROLOGY, (2002 Jul) 168 (1) 93-9.
Journal code: 0376374. ISSN: 0022-5347.
CY United States
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200207
ED Entered STN: 20020619
Last Updated on STN: 20020709
Entered Medline: 20020708
AB PURPOSE: Serum prostate specific **antigen** is a highly specific test for diseases of the prostate gland but it is not specific for prostate cancer, which can lead to unnecessary biopsies. In an effort to find a more specific test, a new testing method for detecting prostate cancer based on **deglycosylation** of cell surface proteins and subsequent antibody formation in patients with prostate cancer was evaluated. In addition, antibody generation against the peptide fragments chosen to represent the cell surface proteins was determined to be **cancer associated, cancer specific** or not related to prostate cancer. MATERIALS AND METHODS: Antibody titers to 67 unique peptide sequences representing 41 cell surface proteins were

determined in 25 men with known prostate cancer (cancer group) and 34 men without prostate cancer (control group). The titers of the control and cancer groups were compared for statistical significance. Additionally, each peptide was identified as being **cancer specific**, **cancer associated** or not related to prostate cancer based on whether patients, controls, both or neither had elevated antibody titers. RESULTS: Of the 67 peptides tested 3 demonstrated statistical significance between the control and cancer group titers. Using these 3 informative peptides, 11 of the 25 men known to have prostate cancer had positive results (sensitivity 44%), while 2 of the 34 control patients had positive results (specificity 94%). Of the peptides with significantly different titers in patients and controls 2 of the 19 cell surface proteins known to be present in prostate cancer were represented. No peptides were found to generate antibodies only in patients with cancer (**cancer specific**), while 3 were **cancer associated** (increased in cancer and controls). CONCLUSIONS: A new approach to testing for prostate cancer, although lacking in sensitivity, appears to be highly specific. The high specificity of this test suggests that when combined with a highly sensitive test, such as prostate specific **antigen**, screening could be significantly improved.

CT Check Tags: Comparative Study; Human; Male
Adult
Aged
*Antibodies, Neoplasm: BL, blood
Antibody Specificity: IM, immunology
***Antigens, Surface: BL, blood**
Biopsy
Middle Age
***Peptide Fragments: BL, blood**
Predictive Value of Tests
Prostate: PA, pathology
Prostate-Specific Antigen: BL, blood
***Prostatic Neoplasms: DI, diagnosis**
Prostatic Neoplasms: IM, immunology
Reference Values
*Tumor Markers, Biological: BL, blood

CN 0 (Antibodies, Neoplasm); 0 (Antigens, Surface); 0 (Peptide Fragments); 0 (Tumor Markers, Biological); EC 3.4.21.77 (Prostate-Specific Antigen)

L121 ANSWER 2 OF 4 MEDLINE
AN **2000463821** MEDLINE
DN **20468866** PubMed ID: **11016651**
TI Use of two predictive algorithms of the world wide web for the identification of tumor-reactive T-cell epitopes.
AU Lu J; Celis E
CS Department of Immunology and Cancer Center, Mayo Clinic and Mayo Graduate School, Rochester, Minnesota 55905, USA.
NC R01CA80782 (NCI)
SO CANCER RESEARCH, (2000 Sep 15) 60 (18) 5223-7.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001013

AB Tumor cells can be effectively recognized and eliminated by CTLs. One approach for the development of CTL-based cancer immunotherapy for solid tumors requires the use of the appropriate immunogenic peptide epitopes that are derived from defined **tumor-associated antigens**. Because CTL peptide epitopes are restricted to specific

MHC alleles, to design immune therapies for the general population it is necessary to identify epitopes for the most commonly found human MHC alleles. The identification of such epitopes has been based on MHC-peptide-binding assays that are costly and labor-intensive. We report here the use of two computer-based prediction algorithms, which are readily available in the public domain (Internet), to identify HL4-B7-restricted CTL epitopes for carcinoembryonic **antigen** (CEA). These algorithms identified three candidate peptides that we studied for their capacity to induce CTL responses in vitro using lymphocytes from HLA-B7+ normal blood donors. The results show that one of these peptides, CEA9(632) (IPQQHTQVL) was efficient in the induction of primary CTL responses when dendritic cells were used as **antigen** -presenting cells. These CTLs were efficient in killing tumor cells that express HLA-B7 and produce CEA. The identification of this HLA-B7-restricted CTL epitope will be useful for the design of ethnically unbiased, widely applicable immunotherapies for common solid epithelial tumors expressing CEA. Moreover, our strategy of identifying MHC class I-restricted CTL epitopes without the need of peptide/HLA-binding assays provides a convenient and cost-saving alternative approach to previous methods.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
***Algorithms**
Amino Acid Sequence
Antibodies, Monoclonal: IM, immunology
Antigen Presentation: IM, immunology
***Carcinoembryonic Antigen: IM, immunology**
Carcinoembryonic Antigen: ME, metabolism
Cell Line, Transformed
Dendritic Cells: IM, immunology
*Epitopes, T-Lymphocyte: IM, immunology
***HLA-B7 Antigen: IM, immunology**
HLA-B7 Antigen: ME, metabolism
Immunotherapy, Adoptive
***Internet**
Lymphocyte Transformation: IM, immunology
Neoplasms: IM, immunology
Neoplasms: TH, therapy
***Peptide Fragments: IM, immunology**
Peptide Fragments: ME, metabolism
Predictive Value of Tests
T-Lymphocytes, Cytotoxic: IM, immunology
Tumor Cells, Cultured

CN 0 (Antibodies, Monoclonal); 0 (Carcinoembryonic Antigen); 0 (Epitopes, T-Lymphocyte); 0 (HLA-B7 Antigen); 0 (Peptide Fragments)

L121 ANSWER 3 OF 4 MEDLINE
AN **97384957** MEDLINE
DN **97384957** PubMed ID: **9242452**
TI T-cell recognition of tumor-associated carbohydrates: the nature of the glycan moiety plays a decisive role in determining glycopeptide immunogenicity.
AU Galli-Stampino L; Meinjohanns E; Frische K; Meldal M; Jensen T; Werdelin O; Mouritsen S
CS M&E Biotech A/S, Valby, Denmark.
SO CANCER RESEARCH, (1997 Aug 1) 57 (15) 3214-22.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19970922
Last Updated on STN: 19970922

Entered Medline: 19970911

AB Aberrant glycosylation is one of the most constant traits of the malignant cell phenotype. To study T-cell responses to **tumor-associated** glycans, the mouse hemoglobin-derived decapeptide Hb(67-76), which binds well to the MHC class II molecule E(k) and is nonimmunogenic in CBA/J mice, was either O- or N-glycosylated at its primary T-cell receptor contact residue, position 72, with different glycans attached to either threonine, serine, or asparagine. The carbohydrate moieties included **tumor-associated** mucins, i.e., the Tn and T **antigens**, mucin-related glycans, and mucin-unrelated glycans. The side chain of the amino acid in position 72 points away from the MHC binding site when the Hb(67-76) peptide is bound to E(k), so the assumption was that this was also the case for glycans attached to this position. The glycosylated Hb(67-76) peptide analogues were then studied for binding to E(k) and for immunogenicity in CBA/J mice. All 16 glycopeptides bound well to E(k), although those with the more complex carbohydrates bound more weakly than those with monosaccharides. Six of 12 O-glycosylated and 0 of 4 N-glycosylated glycopeptides were able to induce a T-cell proliferative response with a stimulation index above 3.0. Some glycopeptides were not immunogenic, suggesting that there may be holes in the T-cell repertoire due to a lack of T-cell receptor regions accommodating certain glycan structures. The four strongest immunogenic glycopeptides were all O-glycosylated, and interestingly, three of them carried the **tumor-associated** Tn or T **antigen**. On the other hand, the Hb(67-76) peptide analogue with the natural mucin Core2 structure attached did not elicit any T-cell response. T cells primed to a glycopeptide with a simple glycan structure such as Tn did not cross-respond significantly to other glycopeptides, indicating a high degree of carbohydrate specificity in T-cell recognition. T cells primed to a glycopeptide carrying the more complex T **antigen** showed a complicated pattern of cross-responses to glycopeptides with simpler glycan moieties. The fact that it is possible to raise MHC class II-restricted T-cell responses against **tumor-associated** carbohydrate structures opens new perspectives for the designing of cancer vaccines.

CT Check Tags: Animal; Support, Non-U.S. Gov't
***Antigens, Tumor-Associated, Carbohydrate: IM, immunology**
Binding, Competitive
Cell Division: IM, immunology
*Glycopeptides: IM, immunology
*Hemoglobins: ME, metabolism
***Histocompatibility Antigens Class II: ME, metabolism**
Mice
Mice, Inbred CBA
Models, Structural
***Peptide Fragments: IM, immunology**
*T-Lymphocytes: IM, immunology
T-Lymphocytes: ME, metabolism

CN 0 (**Antigens, Tumor-Associated,** Carbohydrate); 0 (Glycopeptides); 0 (Hemoglobins); 0 (Histocompatibility Antigens Class II); 0 (Peptide Fragments)

L121 ANSWER 4 OF 4 MEDLINE

AN **95142964** MEDLINE

DN **95142964** PubMed ID: **7840926**

TI Serum immunoglobulins specific for intracellular proteins of squamous cell carcinoma.

AU **Calenoff E**; Cheever M A; Satam M; Dutra J C; Pelzer H J; Kern R C; Hanson D G

CS Department of Otolaryngology and Head and Neck Surgery, Northwestern University Medical School, Chicago, Ill.

SO ARCHIVES OF OTOLARYNGOLOGY -- HEAD AND NECK SURGERY, (1995 Feb) 121 (2) 183-91.

Journal code: 8603209. ISSN: 0886-4470.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199503
ED Entered STN: 19950316
Last Updated on STN: 19970203
Entered Medline: 19950309
AB OBJECTIVE: To determine an autologous humoral immune response to squamous cell carcinoma (SCC) intracellular proteins in patients with SCC. DESIGN: Intracellular proteins were isolated from 25 different cultured SCC lines. The proteins were used as a source of **antigens** to measure IgA, IgE, and IgG responses in the serum samples of patients and controls. Antibody response was assessed in both unfractionated and fractionated intracellular proteins. PATIENTS: The serum samples of 65 patients with SCC and of 65 age- and gender-matched controls were tested. RESULTS: Antibodies to SCC intracellular proteins were detected in the serum samples of 40 (62%) of the 65 patients with SCC and in the serum samples of 46 (71%) of 65 controls. Thirty (46%) of the patients with SCC and 40 (62%) of the controls had IgE responses, 18 (28%) of the patients and one (2%) of the controls had IgA responses, and 17 (26%) of the patients and 14 (22%) of the controls had IgG responses. An inverse relation was noted between detectable IgE responses and IgA or IgG responses in the patients and the controls. The analysis of antibody response indicated that 28 molecules were recognized predominantly by the serum samples of patients with SCC, but not by the serum samples of controls. CONCLUSIONS: A substantial proportion of patients with SCC and of controls exhibited an autologous humoral immune response to SCC intracellular proteins. The IgE responses to SCC intracellular proteins were inversely related to IgA or to IgG responses. Different antibody isotypes normally cause markedly different immune functions, and may suggest different roles for the existent immune responses to SCC **antigens**. We identified many **tumor-associated antigens** that were selectively recognized by the serum samples of patients with SCC. These **antigens** could be used to define molecular studies of immune surveillance and selection, and may represent appropriate targets for immunotherapy.
CT Check Tags: Human
Autoradiography
Blotting, Western
*Carcinoma, Squamous Cell: IM, immunology
*Head and Neck Neoplasms: IM, immunology
Immunoglobulin A: BL, blood
Immunoglobulin E: BL, blood
Immunoglobulin G: BL, blood
*Immunoglobulins: BL, blood
Immunoglobulins: ME, metabolism
Neoplasm Proteins: IM, immunology
Neoplasm Proteins: ME, metabolism
Tumor Cells, Cultured
RN 37341-29-0 (Immunoglobulin E)
CN 0 (Immunoglobulin A); 0 (Immunoglobulin G); 0 (Immunoglobulins); 0 (Neoplasm Proteins)

=> fil wpix
FILE 'WPIX' ENTERED AT 15:23:13 ON 19 NOV 2002
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FILE LAST UPDATED: 18 NOV 2002 <20021118/UP>
MOST RECENT DERWENT UPDATE: 200274 <200274/DW>
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=> d all abeq tech abex tot l136

L136 ANSWER 1 OF 3 WPIX (C) 2002 THOMSON DERWENT
AN **2002-566624** [60] WPIX
DNC **C2002-160592**
TI Candidates for cancer-specific or cancer-associated antigens useful for diagnosis and treatment of cancer comprise synthetic peptides.
DC B04
IN **CALENOFF, E; DITLOW, C C**
PA (NOUN) UNIV NORTHWESTERN
CYC 98
PI WO 2002047613 A2 20020620 (200260)* EN 53p A61K000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002043314 A 20020624 (200267) A61K000-00
ADT WO 2002047613 A2 WO 2001-US47734 20011113; AU 2002043314 A AU 2002-43314 20011113
FDT AU 2002043314 A Based on WO 200247613
PRAI US 2000-723307 20001127
IC ICM A61K000-00
AB WO 200247613 A UPAB: 20020919
NOVELTY - Identifying candidates that are cancer-specific or cancer-associated antigens involves:
(1) mapping hydrophilic regions of amino acid sequences;
(2) identifying hydrophilic peptide regions that are glycosylated in non-cancerous cells, but deglycosylated in cancer cells; and
(3) synthesizing, labeling and testing peptides.
DETAILED DESCRIPTION - Identifying candidates that are cancer-specific or cancer-associated antigens involves:
(a) obtaining the amino acid sequences of the extracellular domain of a receptor or receptor-like molecule;
(b) mapping hydrophilic regions of the domain by analyzing the amino acid sequence of the domain employing the rolling sum analysis of seven consecutive residues;
(c) identifying the hydrophilic peptide regions of step (b) that are glycosylated in non-cancerous (normal) cells, but are deglycosylated in cancer cells;
(d) locating amino acids that are susceptible to modification in the absence of steric hindrance by glycoside chains;
(e) synthesizing candidate peptides that fit the criteria of steps (a) to (d);

(f) labeling the peptides at either end of their amino acid sequence; and

(g) testing whether the candidate peptides are cancer-specific or cancer associated.

INDEPENDENT CLAIMS are included for the following:

(1) a cancer-specific or highly cancer-associated peptide comprising an amino acid sequence containing 3 - 1000 amino acids; a net hydrophilic character; and at least one glycosylatable amino acid located at no further than 3 amino acids away from the amino acid adjacent to either end of the peptide;

(2) an immunogenic composition comprising the peptide and capable of inducing a mammal to produce antibodies specific for an epitope on a cancer cell;

(3) an immunoassay by determining whether the peptide has complexed with an antibody in the biological fluids;

(4) a diagnostic method involving placing several peptides in a microchip to detect cancer in a subject from which a biological sample is obtained, and detecting the cancer by hybridization of antibodies in the biological sample;

(5) a molecule (I) specifically reactive with the peptide, selected from monoclonal antibodies or their immunogenic fragments, recombinant proteins or adhesion proteins;

(6) delivering cancer cell molecules containing epitopes expressed by the peptides for identifying cancer status by an immunoassay for the complexing of the cancer cell with (I);

(7) determining degree of cancer expression or by measuring antibody by the immunoassay;

(8) determining type of cancer cells in a biological sample by complexing of cancer cell molecules with (I);

(9) a cancer imaging reagent comprising (I) and a label;

(10) a therapeutic construct (C1) comprising the peptide, and an adjuvant/peptide conjugates comprising the peptide coupled to a molecule which facilitates enhanced immunogenicity, and neomolecules created by recombinant techniques containing a peptide with adjuvant molecular sequences which promotes increased immunogenicity of the peptide;

(11) a therapeutic construct (C2) comprising a nucleic acid molecule comprising a nucleotide sequence encoding the peptide, expressed as the protein or peptide by the cells of an individual after administration, to cause auto-stimulation of the individuals immune system; and

(12) producing immunity to cancer by administering (C2) to a mammal.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Cancer cell apoptosis promoter.

USE - To identifying candidates that are cancer-specific or cancer-associated antigens for use in the diagnosis and treatment of cancer (claimed)

ADVANTAGE - The method involves the use of a site of deglycosylated amino acid in the cancer cells, thus conferring a cancer-specific or highly cancer-associated immunogenicity or marker function to the peptide and avoiding self-recognition, compared to the prior art peptides. The peptides are further not intracellularly expressed, but are located on the cell surfaces (predictably secreted or released into pericellular fluids) in sufficient numbers, thus are sufficiently accessible for targeting T cells; and are present at the earlier stages of cancer progression as well as during later stages; and are retained on the surface of the cancer cells for a time sufficient for the therapeutic T cells to find their target and retain the bound T cells for a time sufficient to affect cancer cell death.

Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: **B04-B04C; B04-C01; B04-K01;** **B04-N02;** B10-B02; B11-C07B5; B11-C08A; B12-K04A1; **B14-H01B; B14-H03**

TECH UPTX: 20020919
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Peptides: The peptide is immunogenic. The glycosylatable amino acid is asparagine. The peptide further comprising several deglycosylated amino acids, each separated from the deglycosylated amino acid nearest to it by not more than 6 unmodified amino acids. The peptide further comprises: a chemical modification of at least one of the deglycosylated amino acids, such that the chemical modification confers upon the peptide an additional cancer-specific or highly cancer-associated immunogenicity than that due to glycosylation; and an amino acid sequence with not more than 3 unmodified amino acids are located on either side of a modified amino acid or amino acid that has a glycosylation site removed. The chemical modification is phosphorylation. The peptide is produced synthetically.
Preferred Label: The label is radioisotopic and, upon binding to cancer cells cancerous lesion, highlights the presence of the cancer cells when scanned with a nuclear medicine scanner. The cancer imaging reagent contains a paramagnetic label which, upon binding to cancer cells highlights the presence of the cancer cells when scanned with a nuclear magnetic resonance (NMR) scanner; or a water density label which, upon binding to cancer cells highlights the presence of the cancer cells when scanned with a CAT scanner.
Preferred Therapeutic Agents: The cancer therapeutic reagents bind to a cancer cell and promote lysis of that cell; bind to and block the function of a receptor or receptor-like molecule or adhesion molecule on a cancer cell, so as to promote a reduction or cessation of cancer cell growth or migration, or promote cancer cell death; and carry a radioisotope or a toxin which upon binding to a cancer cell damages or promotes cancer cell death.

ABEX
SPECIFIC SEQUENCES - Thirty sequences of amino acids are specifically claimed as suitable candidate cancer antigens, e.g. (uuMuuN)n where u is an unmodified amino acid, N is a deglycosylation amino acid, M is a modified amino acid and n is number of repeats of a basic unit.

EXAMPLE - No relevant example given.

L136 ANSWER 2 OF 3 WPIX (C) 2002 THOMSON DERWENT
AN **2000-579032** [54] WPIX
DNC **C2000-172270**
TI Novel composition comprising deglycosylated fragments of kringle 1-5 regions of plasminogen linked to the glycosylated form, useful for inhibiting angiogenesis.
DC B04 C06 D16
IN FOLKMAN, M J; LIANG, H; MACDONALD, N J; PIRIE-SHEPHERD, S; SIM, K L
PA (CHIL-N) CHILDRENS MEDICAL CENT; (ENTR-N) ENTREMED INC
CYC 90
PI WO 2000047729 A1 20000817 (200054)* EN 42p C12N009-68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000029903 A 20000829 (200062) C12N009-68
EP 1153125 A1 20011114 (200175) EN C12N009-68
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002536458 W 20021029 (200274) 49p A61K038-48
ADT WO 2000047729 A1 WO 2000-US3482 20000210; AU 2000029903 A AU 2000-29903 20000210; EP 1153125 A1 EP 2000-908590 20000210, WO 2000-US3482 20000210; JP 2002536458 W JP 2000-598628 20000210, WO 2000-US3482 20000210
FDT AU 2000029903 A Based on WO 200047729; EP 1153125 A1 Based on WO 200047729; JP 2002536458 W Based on WO 200047729
PRAI US 1999-128062P 19990407; US 1999-119562P 19990210

IC ICM A61K038-48; C12N009-68
ICS A61K038-49; A61P015-00; A61P017-06; A61P027-02; A61P029-00; A61P035-00; A61P035-02; A61P035-04; A61P043-00; C07K014-745; C12N015-09

AB WO 200047729 A UPAB: 20011129
NOVELTY - Composition comprising a deglycosylated fragment (I) of a kringle 1-5 region of a plasminogen (PG) protein that lacks at least 1 carbohydrate moiety linked to (and in a greater amount than) the naturally glycosylated form, where the deglycosylated fragment has antiangiogenic activity, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a nucleotide sequence (II) encoding the deglycosylated fragment of (I);
(2) a deglycosylated fragment of a kringle 1-5 region of a PG protein comprising a sequence of 260 amino acids (aa) (Ia), given in the specification; and
(3) a nucleic acid encoding a deglycosylated fragment of a kringle 1-5 region of a PG protein comprising a sequence of 1679 base pairs (bp) (IIa), given in the specification.
ACTIVITY - Cytostatic; antiangiogenic.
No biological data given.
MECHANISM OF ACTION - Angiostatin agonist.
USE - The compositions are useful for inhibiting angiogenesis (claimed)
DESCRIPTION OF DRAWING(S) - The diagram shows the inhibition of endothelial cell proliferation by glycosylated and deglycosylated kringle 1-5 region proteins.
Dwg.4/4

FS CPI

FA AB; GI; DCN

MC CPI: B04-B03B; B04-C01G; B04-E02B; B04-H01; B04-H0100E; B04-H15; B04-H1500E; B04-N02A; B14-H01B; B14-L06; C04-B03B; C04-C01G; C04-E02B; C04-H01; C04-H0100E; C04-H15; C04-H1500E; C04-N02A; C14-H01B; C14-L06; D05-C12; D05-H12A; D05-H12B; D05-H17A2; D05-H17A6; D05-H17B2; D05-H17B6

TECH UPTX: 20001027
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fragments: (I) lacks a bisialylated-biantennary glycan, an N-linked carbohydrate moiety, and/or a carbohydrate chain at aa Asn289 of human PG (hPG). The fragment is a kringle 1-3 protein. The fragment begins at aa 87 of hPG and preferably comprises (Ia). The fragment has a substitution at aa 289 of hPG. (I) has antiangiogenic activity in vitro and/or in vivo.
Production: The deglycosylated fragment is produced recombinantly.
Preferred Composition: The composition has a ratio of deglycosylated fragment to glycosylated form of at least 60:40 (preferably 100:0).
Preferred Nucleotide: The nucleotide of (II) is (IIa).

ABEX
EXAMPLE - Human plasminogen (hPG) was purified from human plasma according to Brockway W. J. and Castellino, F. J., Arch. Biochem. Biophys. 151:194-199 (1972). The hPG was then applied to a 5 ml conA HiTrap column. PG2 (deglycosylated) does not bind to the column, which was rinsed with 5 column volumes of equilibration buffer (50 mM Tris (RTM) pH7.5/ 1 mM MgCl2/ 1 mM CaCl2) and PG1 (glycosylated) eluted. PG1 and 2 were dialyzed against 20 mM Tris (RTM) pH 7.6 and equal amounts of the glycoforms were then digested with pocine pancreatic elastase (PPE) as in O'Reilly, M. S. et al. Nature Medicine 2:689-692 (1996). The kringle 1-3 region protein was separated from the kringle 4 and other smaller (less than 12 kDa) fragments by gel filtration. Bovine capillary endothelial cells were maintained in Dulbecco's modified Eagle's medium/minimal essential medium (DMEM) with 10 % heat-inactivated BCS (not defined), antibiotics and 3 ng/ml recombinant human bFGF (fibroblast growth factor). Cells were washed with phosphate buffered saline (PBS) and dispersed in a 0.05 % solution of

trypsin. A cell suspension was made with DMEM/ 10 % BCS/ 1 % antibiotics and adjusted to 25000 cells/ml. Cells were plated onto gelatinized culture plates and incubated 37 degrees C in 10 % CO2 for 24 hours. The media was them replaced with 0.25 ml of DMEM/ 1% BCS/ 1 % antibiotics and the test sample (PG1 or PG2) applied. After 20 minutes incubation media and bFGF were added. After a further 72 hours the cells were dispersed in trypsin, resuspended and then counted. The assays shows that PG2 isoforms have a higher inhibitory effect on epithelial cells than PG1.

L136 ANSWER 3 OF 3 WPIX (C) 2002 THOMSON DERWENT
AN **1999-244276** [20] WPIX
DNC **C1999-071294**
TI Liquid formulation of interferon-beta.
DC A96 B04
IN HOFER, H; SCHROEDER, P; SIKLOSI, T; TSCHOEPE, M
PA (RENT) RENTSCHLER BIOTECHNOLOGIE GMBH
CYC 25
PI WO 9915193 A1 19990401 (199920)* DE 51p A61K038-21
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA IL JP KR US
AU 9896276 A 19990412 (199934)
EP 1017413 A1 20000712 (200036) DE A61K038-21
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
KR 2001015599 A 20010226 (200156) A61K038-21
JP 2001517635 W 20011009 (200174) 47p A61K038-21
AU 741300 B 20011129 (200206) A61K038-21
EP 1224940 A1 20020724 (200256) DE A61K038-21
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
EP 1017413 B1 20020925 (200271) DE A61K038-21
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9915193 A1 WO 1998-EP6065 19980923; AU 9896276 A AU 1998-96276 19980923; EP 1017413 A1 EP 1998-950074 19980923, WO 1998-EP6065 19980923; KR 2001015599 A KR 2000-703036 20000322; JP 2001517635 W WO 1998-EP6065 19980923, JP 2000-512562 19980923; AU 741300 B AU 1998-96276 19980923; EP 1224940 A1 Div ex EP 1998-950074 19980923, EP 2002-4883 19980923; EP 1017413 B1 EP 1998-950074 19980923, WO 1998-EP6065 19980923, Related to EP 2002-4883 19980923
FDT AU 9896276 A Based on WO 9915193; EP 1017413 A1 Based on WO 9915193; JP 2001517635 W Based on WO 9915193; AU 741300 B Previous Publ. AU 9896276, Based on WO 9915193; EP 1224940 A1 Div ex EP 1017413; EP 1017413 B1 Related to EP 1224940, Based on WO 9915193
PRAI EP 1997-116562 19970923
IC ICM A61K038-21
ICS A61K009-08; A61K047-18
AB WO 9915193 A UPAB: 19990525
NOVELTY - Stable interferon- beta (I) solution of neutral or slightly acid pH (pH 5-8) is new.
DETAILED DESCRIPTION - Liquid formulations of human (I), that retain at least 80% of in vitro biological activity after storage for 3 months at 25 deg. C, contain up to 25 MU (units)/ml of (I), are buffered to pH 5-8, preferably over 5.5, and are free of human serum albumin (HSA); are buffered to pH 6-7.2 and are free of HSA, or are buffered to pH 5-8, preferably over 5.5, and contain at least one amino acid.
ACTIVITY - Antiviral; antiproliferative; immunomodulatory.
MECHANISM OF ACTION - None given.
USE - Interferons are known as antiviral, antiproliferative and immunomodulatory agents.
ADVANTAGE - The formulations have high stability (of biological activity and of molecular and physical integrity); eliminate the expense of freeze-drying and reconstitution, and do not require potentially hazardous additives (serum albumin or detergents). They may even be stored for a month at 37 deg. C and still retain at least 70% of biological activity. A formulation, of pH 7, contained 50 mM sodium phosphate, 50

mg/ml glycerol, 2 mM methionine and 12.5 MU/ml (I). After 6 months storage at 25 deg. C, recovery of biological activity (assessed conventionally by inhibition of the cytopathic effect of a virus) was 13.4 MU/ml, i.e. 107.2% of the initial value and 172% of a control that had been stored for 6 months at -20 deg. C.
Dwġ.0/0 ·

FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-H05B; B14-A02; B14-G03; B14-H01
TECH UPTX: 19990517
TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred buffer: This is phosphate, citrate and/or acetate at concentration 0.01-1, particularly 0.02-0.2 M, especially phosphate/citrate to provide pH 6-7.2, especially 6.2-6.8.
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred materials: (I) is a glycosylated protein, particularly recombinant material from Chinese hamster ovary cells.
Preferred composition: This is free of HSA, surfactants and, apart from (I), polypeptides of human or animal origin, but may also contain at least one amino acid, particularly methionine at 0.1-4, especially 2 mM. Optionally the formulation also contains at least one agent to adjust osmotic pressure (e.g. mannitol or glycerol); a thickener (e.g. methylcellulose) and a preservative (e.g. thiomersal). Compositions retain chemical integrity (against polypeptide cleavage, oxidation and deglycosylation) and physical integrity (as measured from transmission at 420 nm) after storage for 6 months at 25 degrees Centigrade, and at least 85% of the original biological activity. Preferably the (I) concentration is 3-10 MU/ml.

ABEX
ADMINSTRATION - Formulations are administered orally, parenterally or ophthalmologically at unit doses of 1-25 MU (units).

=> d his

(FILE 'HOME' ENTERED AT 13:45:30 ON 19 NOV 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:45:48 ON 19 NOV 2002
E CALENOFF E/AU
L1 21 S E4,E5
E DITLOW C/AU
L2 9 S E3-E5
E ENTERON/PA,CS
L3 3 S E3-E10
L4 28 S L1-L3
L5 28 S ROLL?(L)SUM(L)ANALY?
L6 0 S (ROLL OR ROLLED OR ROLLING)()SUM
L7 14 S (ROLL OR ROLLED OR ROLLING)(5A)SUM
L8 14 S L7 NOT L5
E MATHEMATICS/CT
L9 10519 S E3-E37
E E3+ALL
L10 10519 S E1
E E2+ALL
L11 10890 S E3-E5
L12 85709 S E2+NT
E MATH/CT
L13 6100 S E10-E38
E E39+ALL
E E2+ALL
L14 224812 S E2+NT
L15 65522 S E3-E5

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                E STATISTIC/CT
L16          8813 S E47-E72
                E E5+ALL
L17          9265 S E4-E6
L18         14026 S E3+NT
                E E46+ALL
L19          1092 S E2,E3,E1
                E E5+ALL
L20         36057 S E2,E1+NT
L21        123450 S E7+NT OR E9+NT OR E11+NT OR E12+NT OR E15+NT OR E17+NT
                E E7+ALL
L22            70 S E4
                E E6+ALL
L23         36057 S E2 OR E1+NT
                E E8+ALL
L24          1019 S E4,E3+NT
                E E5+ALL
L25          2826 S E1
                E COMPUTER PROGRAMCT
                E COMPUTER PROGRAM/CT
                E E5+ALL
L26          3710 S E1
                E E2+ALL
L27         49668 S E1
L28             1 S L4 AND L9-L27
                E PROTEIN MOTIF/CT
                E E4+ALL
L29         35999 S E4+NT
L30         20443 S (PROTEIN# OR PEPTIDE# OR POLYPEPTIDE# OR AMINOACID# OR AMINO
L31          2215 S (PROTEIN# OR PEPTIDE# OR POLYPEPTIDE# OR AMINOACID# OR AMINO
L32          6211 S EXTRACELL? DOMAIN
L33           451 S L32 AND L30
L34            63 S L32 AND L31
L35           773 S L29 AND L32
L36            31 S L33-L35 AND L9-L27
                E SIMULATION/CT
L37        236446 S E3,E5,E6
                E E3+ALL
                E E2+ALL
L38         71733 S E3-E5,E2+NT
                E SIMULATION/CT
                E E5+AKK
                E E3+ALL
L39        235130 S E1
L40             9 S L33-L35 AND L37-L39
L41            35 S L36,L40
L42             7 S L41 AND ANTIGEN?
L43             7 S L41 AND (?CANCER? OR ?NEOPLAS? OR ?TUMOR? OR ?TUMOUR? OR ?MAL
L44        923440 S (PROTEIN# OR PEPTIDE#)/CW
L45        149277 S (AMINO(L)ACID#)/CW
L46        107917 S (AMINO ACID# OR PROTEIN# OR PEPTIDE#)/SC,SX
L47          2955 S L44-L46 AND L32
                E MOLECULAR STRUCTURE/CT
                E E3+ALL
L48        240580 S E2,E1+NT AND L44-L46
L49         15577 S (E232+NT OR E233+NT OR E234+NT OR E236+NT OR E240+NT OR E241+
L50          1530 S E225+NT AND L44-L46
L51         10215 S L47-L50 AND L9-L27
L52           109 S L51 AND GLYCOSYLAT?
L53            13 S L51 AND DEGLYCOSYLAT?
L54            10 S L52 AND L53
                SEL DN AN 2 6
L55             2 S L54 AND E1-E6
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L56           2 S L28,L55
L57           1 S L42,L43  AND L56
L58          11 S L42,L43 NOT L56
                SEL DN AN 6 9
L59           2 S E7-E12
L60           4 S L56,L59 AND L1-L59
L61          27 S L4 NOT L60
                SEL DN AN 3 5 6 8 11
L62           5 S L61 AND E13-E27
L63           9 S L60,L62
L64        2257 S (CANCER? OR TUMOR? OR NEOPLAS?)()SPECIFIC (L) ANTIGEN?
L65        5624 S (CANCER? OR TUMOR? OR NEOPLAS?)()ASSOC? (L) ANTIGEN?
L66        2228 S L64,L65 AND L44-L46
L67          66 S L66 AND GLYCOSYLAT?
L68           4 S L67 AND DEGLYCOSYLAT?
L69          32 S L66 AND L9-L27
L70         125 S L29 AND L66
L71          27 S L66 AND L32
L72           9 S L71 AND L67,L69,L70
L73           1 S L69 AND L71
L74           4 S L69,L71 AND L67
L75          48 S L69,L71 NOT L67,L68,L72-L74
                SEL DN AN 17 29 36
L76           3 S L75 AND E28-E36
L77           7 S L74,L76
L78           7 S L77 AND L1-L77

     FILE 'HCAPLUS' ENTERED AT 14:43:45 ON 19 NOV 2002

     FILE 'BIOSIS' ENTERED AT 14:44:06 ON 19 NOV 2002
                E CALENOFF E/AU
L79          28 S E3,E4
                E DITLOW C/AU
L80          21 S E3-E6
L81          45 S L79,L80
L82          34 S L81 AND (10064 OR 10054)/CC
L83          27 S L82 AND 345?/CC
L84          13 S 12504/CC AND L83
                SEL DN AN 1 2
L85           2 S L84 AND E1-E4
L86          18 S L81 AND 00520/CC

     FILE 'MEDLINE' ENTERED AT 14:50:14 ON 19 NOV 2002
                E CALENOFF E/AU
L87          12 S E3,E4
                E DITLOW C/AU
L88           9 S E3-E5
L89          20 S L87-L88
                SEL DN AN 1 10
L90           2 S E1-E6 AND L89
L91        9728 S L64,L65
                E PEPTIDE FRAGMENT/CT
                E E4+ALL
L92         183 S L91 AND E4+NT
                E REFERENCE VALUE/CT
                E E4+ALL
L93           2 S E4+NT AND L92
                E PREDICT/CT
                E E 9+ALL
                E PREDICT/CT
                E E9+ALL
L94          13 S E81+NT AND L92
L95         151 S C4./CT AND L92
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L96          13 S L93,L94 AND L95
                E TUMOR CELLS/CT
                E E4+ALL
L97          72 S E7+NT AND L92
L98          56 S E8+NT AND L92
L99           7 S L1./CT AND L92
L100         19 S L90,L93,L99,L96 AND L87-L99
                E ANTIGENS, NEOPLAS/CT
                E E4+ALL
L101      50974 S E8+NT
L102        183 S L91 AND PEPTIDE FRAGMENTS+NT/CT
L103          7 S L102 AND L1./CT
                E ANTIGENS, SURFACE/CT
                E E3+ALL
L104     219627 S E8+NT
L105        108 S L102 AND L104
L106         94 S L105 AND C4./CT
L107         40 S L105 AND TUMOR CELLS, CULTURED+NT/CT
L108         98 S L106,L107
L109          1 S L108 AND GLYCOSYLAT?
L110          1 S L108 AND DEGLYCOSYLAT?
L111          3 S L109,L110,L90
L112          2 S L111 NOT BOND/TI
                SEL L103 4 6 DN AN
L113          2 S E1-E6
L114          4 S L112,L113 AND L87-L113
L115         98 S L108 AND D12./CT
                E AMINO ACID MOTIF/CT
                E E4+ALL
L116          4 S E36+NT AND L115
                E MATH/CT
                E E8+ALL
                E STATISTIC/CT
                E E2 9+ALL
                E STATISTIC/CT
                E E29+ALL
L117     991027 S E27+NT
L118       2105 S PEPTIDE FRAGMENTS+NT/CT AND L117
L119         52 S L118 AND L101
L120          6 S L7
L121          4 S L114 AND L87-L120

     FILE 'MEDLINE' ENTERED AT 15:13:54 ON 19 NOV 2002

     FILE 'WPIX' ENTERED AT 15:14:03 ON 19 NOV 2002
                E CALENOFF E/AU
L122         22 S E3,E4
                E DITLOW C/AU
L123          4 S E4
L124         24 S L122,L123
L125          1 S L124 AND (B04-C01? OR C04-C01?)/MC
L126         16 S L124 AND (B04-B04C? OR C04-B04C?)/MC
L127          1 S L124 AND (B04-K01? OR C04-K01?)/MC
L128          3 S L124 AND (B04-N02? OR C04-N02?)/MC
L129          1 S L124 AND (B14-H? OR C14-H? OR B12-G07 OR C12-G07)/MC
L130          2 S L124 AND P63?/M0,M1,M2,M3,M4,M5,M6
L131          2 S L129,L130
L132          1 S L131 NOT HELICOBACTER/TI
L133          1 S L132 AND L122-L132
L134          7 S (P63?/M0,M1,M2,M3,M4,M5,M6 OR (B14-H? OR C14-H? OR B12-G07 OR
                SEL DN AN 2 3 5
L135          3 S E1-E6
L136          3 S L133,L135
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L137 4 S L134 NOT L136

FILE 'WPIX' ENTERED AT 15:23:13 ON 19 NOV 2002